3 ~~14~~. A method of treatment of hypercholesterolemic atherosclerosis which comprises administering to a patient an effective amount of a secoisolariciresinol diglucoside (SDG) metabolite selected from the group consisting of secoisolariciresinol (SECO) enterodiol (ED) and enterolactone (EL) at a purity of at least 90%.

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4 ~~15~~. A method of treatment of diabetes type I or type II, which comprises administering to a patient an effective amount of a secoisolariciresinol diglucoside (SDG) metabolite selected from the group consisting of secoisolariciresinol (SECO) enterodiol (ED) and enterolactone (EL) at a purity of at least 90%.

Pages are also included showing the changes made on page 1 and claim 15.

REMARKS

The claims of this application have been restricted to the treatment of hypercholesterolemic atherosclerosis and diabetes type I or type II. The description has also been amended to incorporate by reference U.S. Patent 5,846,944.

Looking first at the rejection under 35 U.S.C. 112, it is noted that the Examiner has found the specification to be enabling for treatment of hypercholesterolemic atherosclerosis. It is respectfully submitted that by incorporating by reference USP 5,846,944 it is reasonable to also include the treatment of diabetes.

The Examiner has also rejected all claims under 35 U.S.C. 102(a) as being anticipated by or obvious over Clark et al. 5,837,256. As the Examiner points out, Clark et al. discloses a method of treatment of lupus nephritis which comprises administering to a patient an effective amount of secoisolariciresinol or secoisolariciresinol diglucoside (SDG) in substantially pure form.

Lupus nephritis is an auto immune disease and very little is known about the roll of oxygen radicals in this disease. Thus, the teaching of Dr. Clark with regard to lupus nephritis does not serve as a guide for a researcher looking at the treatment of hypercholesterolemic atherosclerosis or diabetes where the role of oxygen radicals is overwhelming. For the uses in accordance with the present invention, it is the antioxidant activity of the metabolites that is important.

It has been known to use Vitamin E in the treatment of hypercholesterolemic atherosclerosis and diabetes type I or type II and, of course, SDG itself was used for this purpose in USP 5,846,944.

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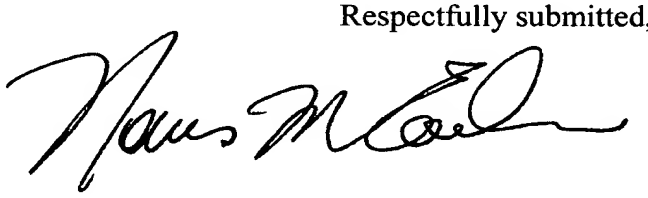
From Figure 3 of the present application, it can be seen that the three metabolites of SDG are vastly more effective as antioxidants than is SDG itself or Vitamin E. There is nothing from the teaching of U.S. 5,846,944 or from Clark U.S.P. 5,837,256 which would have lead a researcher to select the three metabolites of SDG named in the claims of this application as being highly effective antioxidants making them particularly effective for the treatment of hypercholesterolemic atherosclerosis and diabetes type I or type II.

In particular, it could not have been predicted that the metabolites would be so much more effective than is SDG itself. This allows the metabolites to be effectively used in much lower amounts than SDG, thereby further minimizing side effects.

It is, therefore, respectfully submitted that claims 15, 16, 17 and 18 as submitted with this amendment are novel and inventive over Clark U.S. Patent 5,837,256.

Respectfully submitted,



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Version With Markings To Show Changes Made

ANTIOXIDANT ACTIVITY IN SDG METABOLITES

Cross-Reference to Related Application

This application claims the benefit of U.S. Provisional Application No. 60/141,254, filed June 30, 1999.

Background of the Invention

This invention relates to a method for the use of metabolites of secoisolariciresinol diglucoside (SDG) for the treatment of diseases or conditions requiring administration of an antioxidant. These metabolites include secoisolariciresinol (SECO), enterodiol (ED) and enterolactone (EL).

Reactive oxygen species, which include superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (•OH) and singlet oxygen ($^1O_2$), have been implicated in the pathophysiology of numerous diseases, including hypercholesterolemic atherosclerosis, diabetes mellitus, ischemic/reperfusion injury, volume or pressure overload heart failure, hemorrhagic shock, endotoxic shock, ageing, inflammatory bowel disease (Crohn's disease, ulcerative colitis), Parkinson's disease, rheumatoid arthritis and stroke.

Antioxidants such as vitamin E, secoisolariciresinol diglucoside (SDG), probucol, vitamin C, superoxide dismutase, catalase, sulphasalazine, and various other drugs without antioxidant activity, have been shown to be effective to a varying degree in the diseases referred to above. These drugs, with the exception of vitamin C and E and SDG, are expensive and have adverse side effects.

As described in Prasad, U.S. Patent 5,846,944, incorporated herein by reference, SDG, isolated from flaxseed, has been shown to be effective in lowering cholesterol, and in reducing the development of atherosclerosis in hypercholesterolemic rabbits. It is also effective in reducing the incidence of diabetes mellitus and preventing endotoxic shock.

Summary of the Invention

Reactive oxygen species are known to be involved in the pathophysiology of ageing and numerous diseases, such as hypercholesterolemic atherosclerosis, type I and

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Claims

[2. A method according to claim 15 wherein said disease is hypercholesterolemic atherosclerosis.]

[3. A method according to claim 15 wherein said disease is diabetes type I or type II.]

[4. A method according to claim 15 wherein said condition is ischemic heart disease.]

[5. A method according to claim 15 wherein said condition is volume or pressure overload heart failure.]

[6. A method according to claim 15 wherein said condition is the prevention of myocardial injury during open heart surgery.]

[7. A method according to claim 15 wherein said condition is the prevention of restenosis following persutaneous transluminal coronary angioplasty (PTCA).]

[8. A method according to claim 15 wherein said condition is hemorrhagic or endotoxic shock.]

[9. A method according to claim 15 wherein said condition is ageing.]

[10. A method according to claim 15 wherein said disease is inflammatory bowel disease (Crohn's disease, ulcerative colitis).]

[11. A method according to claim 15 wherein said disease is Parkinson's disease.]

[12. A method according to claim 15 wherein said disease is rheumatoid arthritis.]

[13. A method according to claim 15 wherein said disease is stroke.]

15. A method of treatment of a disease or a condition selected from the group consisting of hypercholesterolemic atherosclerosis[,] and diabetes type I or type II, [ischemic heart disease, volume or pressure overload heart failure, prevention of myocardial injury during open heart surgery, prevention of restenosis following persutaneous transluminal coronary angioplasty (PTCA), hemorrhagic or endotoxic shock, ageing, inflammatory bowel disease, Parkinson's disease, rheumatoid arthritis and stroke,] which comprises administering to a patient an effective amount of a secoisolariciresinol diglucoside (SDG) metabolite selected from the group consisting of secoisolariciresinol (SECO) enterodiol (ED) and enterolactone (EL).

16. A method according to claim 15 wherein the metabolites are used at a purity of at least 90%.